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Obese Adolescents Show Reduced Cognitive Processing Speed Compared with Healthy Weight Peers

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Abstract

Background: Childhood obesity and obesity-associated diabetes and metabolic syndrome (MetS) continue to rise. Obesity has been linked to structural and functional brain abnormalities, particularly in the frontal lobe.

Methods: One hundred sixty-two adolescents (aged 19.53 ± 1.53 years) underwent medical, neurocognitive, and brain magnetic resonance imaging assessments. Participants were either healthy weight (BMI <25.0 kg/m^2 or BMI percentile <85%) or obese (BMI ≥30.0 kg/m^2 or BMI percentile ≥95%). We evaluated frontal lobe cognitive functions and the size of the corpus callosum (CC).

Results: Groups differed on four measures of processing speed contained in four different cognitive tests, but not on executive function. A confirmatory factor analysis verified that the significant processing speed variables loaded on the same factor. We also found differences between the weight groups on the area of the anterior portion of the CC, but not the overall CC. Only the Controlled Oral Word Association Test (COWAT) was significantly correlated with the area of the anterior portion of the CC. In the obese group, 32.4% met criteria for MetS. No differences were found between obese participants with or without MetS and none of the MetS factors contributed consistently to cognitive performance.

Conclusions: Obese adolescents show slower cognitive processing speed while maintaining equivalent performance on executive functioning compared with their healthy weight peers. The group differences in the anterior portion of the CC, responsible for frontal lobe interhemispheric communication, may in part explain our processing speed findings. Future studies should include a longitudinal design and diffusion tensor imaging to examine the integrity of white matter.

Keywords: cognition; corpus callosum; obesity; processing speed

Background

The childhood obesity epidemic continues unabated, with 20.6% of US adolescents between the ages of 12 and 19 meeting criteria for obesity during the period 2013–2014.[1] With the rise in obesity in youth, there has been a concurrent increase in metabolic syndrome (MetS).[2–5] MetS is a clustering of risk factors for cardiovascular disease and type 2 diabetes[6] that include dyslipidemia, hypertension, elevated fasting glucose or insulin resistance (IR) (depending on the definition used), and central adiposity. Extant literature in youth documents associations between obesity and adverse medical conditions (*i.e.*, type 2 diabetes, MetS, or sleep apnea)[7–9] and structural brain abnormalities.[10,11]

Adolescent obesity has been associated with decreased performance on tests of executive functions,[12] including attention and set shifting,[13,14] inhibitory control,[15] abstract reasoning, and visuospatial organization.[16] Increased BMI has been linked with decreased general intellectual ability and lower academic achievement in several large nonclinical samples of school-aged children.[17–20] MetS and individual factors of MetS are also associated with reduced neurocognitive performance in adolescents as described in a recent review of the literature.[11]

Processing efficiency is typically assessed by the time taken to correctly make perceptual/cognitive decisions or the number of correct decisions made within a set time.[21] Processing speed provides an indication of the performance efficiency of basic cognitive operations that underlie other

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more complex cognitive and intellectual functions, which can have considerable effects on overall cognitive performance, especially when there are time limitations (*i.e.*, classroom test taking situations). Processing speed reflects coordinated activity across multiple neural networks spanning stimulus perception, motor skills, decision-making, and planning, as well as monitoring of performance.[22] Using a computerized neuropsychological screening battery, a Turkish group found significant differences between obese and healthy weight children aged 8 to 16 years in all assessed domains, including processing speed.[23]

Executive functioning (EF) comprises a diverse set of higher order cognitive abilities associated with self-regulation, decision-making, and goal-directed behavior. Particular components of EF, dependent upon quickness of thinking, multitasking, and processing related to goal-directed behavior, and control of complex cognition, may depend on processing speed.[24] Developmental cognitive and functional imaging studies have shown that adolescence is a period characterized by relative immaturity of executive control systems.[25] Specifically, the prefrontal cortex and associated executive control skills continue to mature through young adulthood.

Reductions in white matter integrity have been associated with diminished performance on attention and processing speed in both adults and adolescents with obesity.[20,26,27] The largest bundle of white matter tracts in the brain is the corpus callosum (CC), which connects the two hemispheres and facilitates the connection of brain networks for cognition.[28] Xu et al.[29] found that BMI was inversely related to white matter integrity in the CC and the fornix. Higher order cognitive processes such as EF are reliant on lower order cognitive functions such as attention and processing speed. Processing speed is impaired in individuals with agenesis of the CC and this has been shown to be related to executive function performance.[30]

The goal of this study was to ascertain the relationships between excess weight and frontal lobe-mediated cognitive performance, including EF, attention, and processing speed, during adolescence when these cognitive functions are maturing. Including attention and processing speed is important as they are crucial to the integrity of higher order EF processes, and also may help explain reported educational performance and cognitive functioning differences among weight groups. We hypothesized that obese participants would have lower scores on tests of attention, processing speed, and EF than their matched healthy weight peers.

Methods

One hundred sixty-two participants were included in a study of obesity and IR in adolescents and young adults. Exclusion criteria included neurological disorder, significant head trauma, psychiatric illness (including substance abuse), or a history of significant medical conditions not associated with obesity. IR, polycystic ovary disease, dyslipidemia, and hypertension were not exclusionary, but type 2 diabetes was. All participants (or their parent/guardian if under 18 years of age) gave written consent (or assent if under 18) to participate in the study and were compensated for their participation. The study was approved by the local Institutional Review Board.

Participants were predominantly recruited through online advertisement or were referred by other study participants. Participants underwent a comprehensive evaluation that included medical, neurological, cognitive, and brain magnetic resonance imaging (MRI) assessments. All recruited participants belonged to one of two nonoverlapping groups based on BMI or BMI percentile if under 18 years of age as follows: healthy weight (BMI $<25.0\,kg/m^2$ or BMI percentile <85%) or obese (BMI $\geq 30.0\,kg/m^2$ or BMI percentile ≥95%). Blood pressure was taken twice during one visit and then the values were averaged. A fasting blood sample was obtained in the morning of one visit and assayed for glucose, insulin, and cholesterol values at NYU Langone Medical Center Outpatient Laboratories. Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated using the following formula: glucose (mg/dL) × insulin (mU/L)/405. Socioeconomic status was assessed using the Hollingshead index.[31] MetS factors were defined using the following criteria: (1) central adiposity (waist circumference at the 90th percentile or higher for age and sex), (2) hypertriglyceridemia (triglyceride level ≥110 mg/day), (3) low high-density lipoprotein cholesterol (HDL) (≤40 mg/dL), (4) elevated blood pressure (for children ≤18 years, a systolic or diastolic blood pressure exceeding the 90th percentile adjusted for age, sex, and height or ≥130/85 mmHg, whichever is lower; for those older than 18 years, ≥130/85 mmHg), and (5) HOMA-IR of 3.99 or higher.[32]

Neuropsychological Assessment

Participants were administered a comprehensive battery of neuropsychological tests identified to assess all primary domains of cognitive functions as well as effort. All tests were administered under standardized conditions, split into two 1.5- to 2-hour sessions. Tests were administered by psychometrists carefully trained and supervised by a licensed neuropsychologist. Because we hypothesized that obese subjects would have lower scores on tests of frontal lobe integrity and EF, we restricted our analysis to tests assessing those domains as well as a test of sustained attention, which can influence overall performance. Estimated full-scale IQ was derived using the Wechsler Abbreviated Scale of Intelligence (WASI).[33] Frontal lobe function was assessed with the following speeded tasks: Controlled Oral Word Association Test (COWAT), Stroop Task,[34] Trail Making Test,[35] Digit Symbol Substitution Test (DSST),[36] and the Letter Number Sequencing subtest from the Wechsler Memory Scale-III.[37] Executive function was assessed by the Tower of London (TOL)[38] and the Category Test (CT),[39] measures that have no speed element, as well as by Trail Making B–Trail Making A, which provides a more pure assessment of EF by eliminating the timed component. Sustained attention was measured with the Digit Vigilance Test (DVT).[40] Effort was assessed

through Green's Medical Symptom Validity Test (MSVT)[41] and Non-Verbal Medical Symptom validity test (NV-MSVT),[42] as well as embedded measures in the CT (number of errors on subtest one and Bolter Validity Index).[43]

MRI Acquisition

All participants were studied on the same 3.0T Siemens Trio System utilizing an identical protocol that had been programmed on the console. The magnetization-prepared rapid acquisition gradient echo (MPRAGE; TR 2300 ms; TE 2.3 ms; TI 1100 ms; FOV 240 × 240; slice thickness 0.90 mm; flip angle 12°; matrix size 256 × 256; 192 coronal slices) sequence was used to estimate the size of the CC. To rule out primary neurological disease, the fast fluid-attenuated inversion recovery (FLAIR; TR 9000 ms; TE 81 ms; FOV 220 × 220; one average and three concatenations; flip angle 120°; slice thickness 3 mm; matrix size 256 × 256; 60 axial slices) sequence was acquired. Although we have cognitive data on 162 participants, 23 of them did not have MRI data because they either failed to keep their MRI appointments ($n = 20$), had claustrophobia ($n = 2$), or were too large to fit in the MRI gantry ($n = 1$). This resulted in 93 obese and 46 nonobese participants with usable brain MRI evaluations.

CC segmentation and parcellation. We used an automated method for computing regional CC areas; for a detailed description of the segmentation method, please refer to Ardekani et al.[44] The subregions of the CC were defined following the method proposed by Hampel et al.[45] These measurements resulted in an overall measure of the CC surface area as well as that of five subregions: C1-rostrum, C2-anterior truncus, C3-middle truncus, C4-posterior truncus, and C5-splenium.

Statistical Analyses

We conducted two-tailed independent sample *t*-tests to examine group differences on demographics, cognitive data, and brain variables. The Mann–Whitney *U* test was used for variables that were not normally distributed (*i.e.*, triglycerides). Chi-square was used to compare race and sex. Factor analysis is a statistical procedure that can be utilized to ascertain which variables cluster together. Because we had *a priori* determined which variables would reflect cognitive processing speed, we conducted a confirmatory factor analysis to verify the loading of the cognitive test scores onto distinct factors such as processing speed and executive function.[46,47] All test scores are initially calculated as raw scores and tests vary for which demographic variables are corrected. For example, WASI, WAIS-R, WAIS-III, Stroop, and TOL scores were corrected for age, whereas the COWAT was corrected for both education and sex, and the Category Test for age, education, and sex. Scores for the DVT were adjusted for age and education.[48]

Because regional brain areas vary in relation to head size, we residualized the overall area of the CC to the intracranial vault (ICV) size through linear regression (saving the unstandardized residual). Furthermore, to determine the CC subregions, we residualized them to the overall CC area and utilized these residual values in statistical analyses. To allow comparability with other studies and to give the reader an idea of the actual areas, we present raw values in the table included in the Results section, but all analyses utilized the residualized values. Stepwise regression analyses were conducted to ascertain the contribution of the five MetS factors (waist circumference, HDL triglycerides, HOMA-IR, and blood pressure) MetS factors were entered simultaneously as independent variables for each of the cognitive scores or brain variables, which differed between weight groups, in turn, as the dependent variable. We controlled for sex in the model testing HDL and waist circumference as those variables have separate cut scores by sex.

Results

There were no differences between healthy and obese weight groups on age, sex, education, socioeconomic status, or estimated full-scale IQ. Indices of effort were consistent with effortful performance for all participants and there were no group differences on effort. As anticipated, the healthy weight and obese groups differed significantly on BMI, HOMA-IR (an index of IR),[49] fasting glucose (although all in the normal range), fasting insulin, HDL, triglycerides, C-reactive protein (a measure of inflammation), and waist circumference (Table 1).

From eight separate cognitive tests, we computed 11 variables of frontal lobe function reflecting executive function, attention, and processing speed. Of these 11 variables, four, which were derived from four separate cognitive tests, differed significantly between the obese and healthy weight groups (although with small to medium effect sizes): DSST, Stroop Word (trial 1), DVT Total Time, and COWAT (Table 2). Each of these four cognitive tests taps a unique frontal lobe function and is considered a type of processing speed; all are timed. The DSST, Stroop, and COWAT measure the number of items correctly completed in a set amount of time. DVT measures the length of time for task completion.

We conducted a confirmatory factor analysis to verify that the variables observed to be significant in the univariate comparisons loaded onto the same factor. The results of the factor analysis are contained in Table 3. The factor analysis yielded two components. All four variable scores that were significantly different between the groups loaded on Factor 1. Factor loadings for these four variables were fairly high (ranging from 0.621 to 0.763). Factor 1 was significantly different between the groups ($p = 0.009$). In addition to those four variables, Factor 1 also contained Trails A and two other variables derived from the Stroop Task. Importantly, these two additional Stroop variables, which had not differed on the univariate weight group analyses, also have a timed element, thus supporting our premise that Factor 1 reflects processing speed.

Table 1. Demographics

	Healthy weight ($N = 54$)		Obese ($N = 108$)			
	Mean	SD	Mean	SD	p	Cohen's d
Estimated full-scale IQ	105.71	12.83	103.23	11.48	0.241	0.21
Age (years)	19.39	1.52	19.60	1.54	0.410	−0.14
Sex (% female)	53.7		63		0.257	
Education (years)	12.69	1.55	12.87	1.45	0.456	−0.13
Socioeconomic status	3.42	1.05	3.11	1.23	0.120	0.26
BMI (kg/m^2)	21.45	1.87	35.57	4.97	<0.001	−3.36
HOMA-IR index	1.45	0.71	3.69	2.23	<0.001	−1.20
Fasting glucose (mg/dL)	80.76	5.76	86.87	7.4	<0.001	−0.89
Fasting insulin (μIU/mL)	7.33	3.68	17.14	9.64	<0.001	−1.20
HDL (mg/dL)	59.87	13.34	48.43	10.31	<0.001	1.00
Triglycerides (mg/dL)	67.33	29.36	94.58	43.68	<0.001	−0.32[a]
Systolic blood pressure (mmHg)	104.84	8.90	114.20	10.14	<0.001	−0.96
Diastolic blood pressure (mmHg)	62.27	7.90	68.00	7.73	<0.001	−0.74
Mean arterial blood pressure	76.46	7.33	83.40	7.56	<0.001	−0.93
Waist circumference (cm)	78.47	6.20	112.15	14.62	<0.001	−3.43

[a]Because triglycerides were not normally distributed, a Mann–Whitney U test was used to compare groups, therefore this effect size is an r, not a Cohen's d.
HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment of insulin resistance.

Because these tasks are more than pure processing speed and likely involve interhemispheric coordination, we hypothesized that the CC may also be compromised and potentially contribute to the slower processing speed. Although we could not reject the null hypothesis for weight group differences in the overall (residualized to ICV size) CC area, supporting our hypotheses, we found significant weight group differences in the area of the anterior (rostrum) portion of the CC (CC1), the area most important for integrating functions across hemispheres for frontal tasks. No other

Table 2. Cognitive Results

	Healthy weight ($N = 54$)		Obese ($N = 108$)			
	Mean	SD	Mean	SD	p	Cohen's d
COWAT T score[a]	57.34	10.11	52.11	9.37	0.001	−0.45
Digit Vigilance (residualized to age and education)[a]	−24.61	70.27	10.92	81.89	0.007	0.54
DSST (total score)[a]	65.80	11.92	61.82	10.04	0.027	0.37
Stroop Word T score[a]	45.98	7.68	43.29	7.61	0.036	0.35
Stroop Color T score	45.77	6.85	44.17	8.42	0.227	0.20
Stroop Color/Word T score	53.65	10.77	50.41	10.62	0.931	0.30
Tower of London—excess moves	10.40	9.15	10.65	10.06	0.885	−0.03
Trails A (seconds)	24.61	9.29	25.59	8.51	0.503	−0.11
Trails B–Trails A (seconds)	34.33	28.31	36.86	23.35	0.546	−0.10
Letter/Number sequencing (total score)	11.09	2.58	11.14	2.15	0.904	−0.02
Category test-adjusted T score	48.22	15.70	50.76	14.09	0.304	−0.17

[a]Significantly different between groups through t-test.
COWAT, Controlled Oral Word Association Test; DSST, Digit Symbol Substitution Test.

Table 3. Confirmatory Factor Analysis

	Factor	
Cognitive variable	**1**	**2**
DSST total score[a]	0.740	0.317
COWAT T score[a]	0.627	0.063
Digit Vigilance (residualized to age and education)[a]	–0.621	0.257
Stroop—Word T score[a]	0.763	0.156
Stroop—Color T score	0.781	0.218
Stroop—Color/Word T score	0.684	0.359
Trails A time (seconds)	–0.521	–0.284
Trails B–Trails A	–0.347	–0.497
Letter/Number sequencing	0.157	0.650
Tower of London—excess moves	–0.039	–0.589
Category test adjusted T score	0.083	0.765

[a]Significantly different between groups through *t*-test.

subregion of the CC was significantly different between the groups (Table 4).

We used Pearson correlations to test the relationship between CC1 and the four significant variables of processing speed as well as Factor 1. We found that only the COWAT T score was significantly correlated with CC1 ($r = 0.217$, $p = 0.010$).

Within the obese group, 32.4% met criteria for MetS. There were no differences between obese participants with and without MetS on any of the cognitive test variables that differed between weight groups. Furthermore, in stepwise regressions, none of the five MetS components were consistently associated with any of the four significant cognitive variables, Factor 1, or CC1 area.

Table 4. Corpus Callosum Differences Between Groups (in cm^2)

	Healthy weight ($N = 46$)		Obese ($N = 93$)			
	Mean	**SD**	**Mean**	**SD**	***p***	**Cohen's *d***
Corpus callosum total area	584.98	74.15	595.79	94.71	0.356	–0.17
CC1	184.55	26.06	182.11	28.68	0.038	0.38
CC2	85.96	14.96	86.74	17.77	0.566	0.10
CC3	66.30	12.99	69.28	16.83	0.366	–0.16
CC4	69.04	17.77	73.72	20.13	0.207	–0.23
CC5	179.14	22.96	183.94	28.31	0.435	–0.14

Conclusions

We found significant differences between obese and healthy weight adolescents in performance on 4 of 11 cognitive variables derived from four unique cognitive tests of frontal lobe function. Each of the significant variables reflected cognitive performance speed. These findings are consistent with those in the literature documenting cognitive deficits in obesity. We did not find weight group differences in EF among our adolescent participants. This is in keeping with the sparse extant literature in this group, which has shown inconsistent findings.

Although all four cognitive test scores that separated our weight groups are timed and generally accepted as measures of processing speed in the neuropsychological literature, we ascertained that they clustered together by means of a confirmatory factor analysis, including all the variables we had selected for analysis. Indeed, all four variables loaded onto Factor 1. In addition to those four variables, Factor 1 also contained Trails A and two other test scores derived from the Stroop Task. Importantly, these two additional Stroop-derived variables, which had not differed on the univariate weight group analyses, also have a timed element, thus supporting our premise that Factor 1 reflects processing speed. Although we had expected Trail Making A to also vary between our groups, it likely did not because it is the least demanding of all the tests and thus may not be challenging enough to expose group differences.

Several groups, including ours, have described structural brain differences between healthy weight and obese individuals.[11] Extant literature describes white matter reductions, including CC, among adults with obesity.[26,29] Preliminary white matter findings have been reported in adolescents.[50] We report that as predicted, the anterior portion of the CC (CC1), which is responsible for connecting the hemispheres at the level of the frontal lobes, was smaller in the obese group. However, while differing between our adolescent weight groups, it did not explain the overall group differences in processing speed. Only the COWAT T score, which (although a measure of processing speed) is a very sensitive measure of frontal lobe integrity,[51] was associated with CC1 (shared 4.7% of variance). Because processing speed and attention are distributed fairly broadly in the brain, despite concentration in the frontal lobes, this may explain the lack of further association between our cognitive and CC measures.

We know that obesity-related comorbidities such as those associated with MetS have been associated with cognitive deficits.[11] However, we did not find a significant contribution of any MetS risk factors, singly or in combination with any of the four cognitive variables, Factor 1, or CC1 area. In a multivariate model (all five MetS factors entered together since they are correlated), only waist circumference and triglyceride level had weak associations each with one of the four processing speed variables separating the groups. This lack of consistent associations is likely due to the varying MetS criteria met by different individuals from individual differences and variability in their degree of excess weight.

This study's strengths include demographically well-matched groups, relatively large sample size, and neuropsychological assessments using standardized measures. The most important limitation of this study is its cross-sectional nature. Because of the individual variability in rates of maturation of the frontal lobe during adolescence as well as the differences in obesity trajectories across study participants, a longitudinal approach would be preferable to better understand the interaction of neuronal maturation, obesity, and cognition. Future studies may also incorporate metabolic markers such as inflammation and sleep apnea as they may identify extant metabolic factors in explaining differences in processing speed. In addition, more sensitive assessments of white matter integrity such as diffusion tensor fractional anisotropy imaging data would be useful to further explore whether there are more diffuse white matter abnormalities than those suggested by our more global CC area measurements.

We found evidence of processing speed differences in obese adolescents compared with their healthy weight peers, but no differences on executive function measures. Given the importance of processing speed in underlying part of executive function performance, our lack of EF dysfunction among obese adolescents suggests they can compensate for the reduction in processing speed while still maintaining normal executive function. Interhemispheric connection is distributed topographically in the CC. We know that the frontal lobes are important in processing speed and executive function and that the anterior aspects of the CC connect the frontal lobes. Therefore, it was not surprising that the only CC subregion distinguishing the weight groups was the anterior portion (CC1), which would be in keeping with our reductions in processing speed, which are partly dependent on frontal lobe integrity and interhemispheric communication. The fact that we only had one of our measures of processing speed associated with CC1 likely reflects the lack of sensitivity of the CC measure in detecting white matter pathology. Future studies should assess white matter health through the much more sensitive diffusion tensor imaging to confirm this possibility.

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Author Disclosure Statement

No competing financial interests exist.

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